

**COMPREHENSIVE GERIATRIC ASSESSMENT IN OLDER PEOPLE:
AN UMBRELLA REVIEW OF HEALTH OUTCOMES**

Short title: UR CGA

Nicola Veronese, Carlo Custodero, Jacopo Demurtas, Lee Smith, Mario Barbagallo, Stefania Maggi, Nicola Vanacore, Luigi Ferrucci, Alberto Pilotto on behalf of the special interest group in Systematic Reviews and Meta-analyses and Comprehensive Geriatric Assessment of the European Geriatric Medicine Society (EuGMS)

KEY POINTS

- Comprehensive geriatric assessment is available to geriatricians and other medical and non-medical figures from three decades, but it is still poorly used.
- Our umbrella review including systematic reviews regarding comprehensive geriatric assessment in older people supported the use of this approach across several settings and clinical situations, even if supported by different degrees of evidence and strength.
- A solid literature supports the use of comprehensive geriatric assessment in hospital medical setting for multiple health outcomes, with a high certainty of evidence, whilst the evidence of benefits is less strong for the use of this approach in other settings.

ABSTRACT

Background: Comprehensive geriatric assessment (CGA) has been in use for the last three decade. However, some doubts remain regarding its clinical use. Therefore, we aimed to capture the breadth of outcomes reported and assess the strength of evidence of the use of comprehensive geriatric assessment (CGA) for health outcomes in older persons.

Methods: Umbrella review of systematic reviews of the use of CGA in older adults searching in Pubmed, Embase, Scopus, Cochrane library and CINHAL until 05th November 2021. All possible health outcomes were eligible. Two independent reviewers extracted key data. The grading of evidence was carried out using the GRADE for intervention studies, whilst data regarding systematic reviews were reported as narrative findings.

Results: Among 1,683 papers, 31 systematic reviews (19 with meta-analysis) were considered, including 279,744 subjects. Overall, 13/53 outcomes were statistically significant ($p < 0.05$). There was high certainty of evidence that CGA reduces nursing home admission (risk ratio [RR]=0.86; 95% confidence interval [CI]: 0.75-0.89), risk of falls (RR=0.51; 95%CI: 0.29-0.89), and pressure sores (RR=0.46; 95%CI: 0.24-0.89) in hospital medical setting; significantly decreases the risk of delirium (OR=0.71; 95%CI: 0.54-0.92) in hip fracture; decreases the risk of physical frailty in community-dwelling older adults (RR=0.77; 95%CI: 0.64-0.93). Systematic reviews without meta-analysis, indicate that CGA improves clinical outcomes in oncology, haematology, and in emergency department.

Conclusions: CGA seems to be beneficial in the hospital medical setting for multiple health outcomes, with a high certainty of evidence. The evidence of benefits is less strong for the use of CGA in other settings.

Key words: comprehensive geriatric assessment; older people; umbrella review.

BACKGROUND

Comprehensive geriatric assessment (CGA) may be considered as a multidisciplinary diagnostic process aimed at identifying medical, psychosocial, and functional needs of older people that guide the development of a coordinated plan to manage the health complexity and to maximize overall health in older persons. [1, 2] Overall, CGA is usually initiated through a referral by the primary care physician or by clinicians working in the hospital setting. For this reason, CGA may be different according to the different settings of care and may impact on different outcomes. [3]

CGA has been studied for approximately three decades.[1] Evidence from randomized controlled trials (RCTs) and meta-research has suggested that CGA significantly improves outcomes in older patients across different conditions and settings.[4] For example, home CGA programs and CGA performed in the hospital have been shown to be consistently beneficial for several health outcomes[5], but results on the effectiveness of post-hospital discharge CGA programs, outpatient CGA consultation, and CGA-based inpatient geriatric consultation services are conflicting. [5] It has been widely recognized that the effectiveness of CGA programs may vary in different settings or specific clinical conditions suggesting CGA programs should be tailored to the specific purposes that they are for, such as preoperative assessment [6], admittance or discharged from emergency departments [7], orthogeriatric units [8] or evaluation of patients with specific medical conditions such as cancer. [9]

Since the body of research on this topic is rapidly expanding, we aimed to summarize the current knowledge of CGA using an umbrella review methodology to capture the breadth of outcomes reported and globally assess strength of evidence that CGA can improve multiple health outcomes in older persons.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) recommendations guidelines were used to guide this umbrella review. [10] The full protocol is available in PROSPERO (CRD42021246239).

Data sources and searches

We searched Pubmed, Embase, Scopus, Cochrane library and CINHALL from database inception until 05th November 2021, with the search strategies reported in **Supplementary Table 1** for systematic reviews with or without meta-analysis in older people using CGA versus standard/usual care or using CGA-based tools for predicting health outcomes of interest.

Study selection

For the aims of this work, we included: 1. systematic reviews with or without meta-analysis that evaluated observational studies with longitudinal (prospective or retrospective) design reporting on health outcomes in subjects receiving CGA, for a given condition, in older people; 2. systematic reviews with or without meta-analysis that evaluated intervention studies, i.e., RCTs comparing CGA versus standard/usual care or no intervention, for a given condition, in older people. We excluded cross-sectional studies, narrative reviews without a formal search of the literature, conference abstracts, meta-analyses that reported less than two studies for a single outcome, and letters to the editor. When more than one systematic review on the same research question was available that used similar study design (observational or RCTs), the one with the largest number of studies was selected.

Data extraction

Two reviewers (JD, CC) independently screened title/abstracts for eligibility, and when a consensus was not reached a third senior reviewer (NV) was consulted. The full texts of potentially eligible

articles were retrieved, and two investigators (JD, CC) independently scrutinized each study for eligibility. When consensus was not reached, a third senior reviewer was consulted (NV).

The following information for each eligible work was extracted: first author name; publication year; number of included studies and number of participants; study population; type of effect size used; study design (RCT or observational); type of CGA by model/setting of delivery (e.g. geriatric ward, geriatric consultation team, acute geriatric care unit, emergency department interventions, pre- or perioperative CGA in non-orthopedic surgical ward, geriatric trauma consultation, geriatric rehabilitation team, orthogeriatric care, multidimensional preventive home visit program); setting; number of participants with (cases) and without (controls) events in observational studies and people randomized to CGA or usual/standard care in RCTs. We also extracted the study-specific estimated relative risk for health outcomes (risk ratio, RR; odds ratio, OR; mean difference, MD; standardized mean difference, SMD) and 95% confidence intervals (CIs). We finally extracted the data for the Assessment of Multiple Systematic Reviews (AMSTAR)-2 tool. [11]

Quality assessment

Two reviewers (CC, JD) assessed the methodological quality of the included meta-analyses using AMSTAR-2 [11, 12] that ranks the quality of a meta-analysis from critically low to high according to sixteen predefined grades. For narrative systematic reviews, no quality assessment was carried out since no validated tools exist for this purpose.

Data synthesis and analysis

For each meta-analysis, we estimated the summary effect size and its 95% confidence interval (CI) by using the random-effects DerSimonian and Laird (DL). [13] We also estimated the prediction interval (PIs) and its 95% CI, which further accounts for between-study effects and estimates the certainty of the association if a new study addresses that same association.[14, 15] Between-study

inconsistency was estimated with the I^2 metric, with values between 50% and 75% indicative of high heterogeneity and $\geq 75\%$ indicating very large heterogeneity.[16] We calculated the evidence of small-study effects (i.e. whether small studies inflated effect sizes). We used the regression asymmetry test [17], using a p-value < 0.10 with more conservative effects in larger studies as indicative of small-study effects.[18] Furthermore, we assessed if the largest study in each meta-analysis in terms of participants was statistically significant, using a p-value < 0.05 .

Finally, we applied the excess of significance test.[19] The larger the difference between observed (O) and expected (E) number of studies, the higher the degree of excess significance. Because of the limited statistical power of this test, a lenient significance threshold ($p < 0.10$) was adopted. [20]

All analyses were conducted with STATA 13.0 (Stata Corp LP, College station, Texas).

Grading the evidence

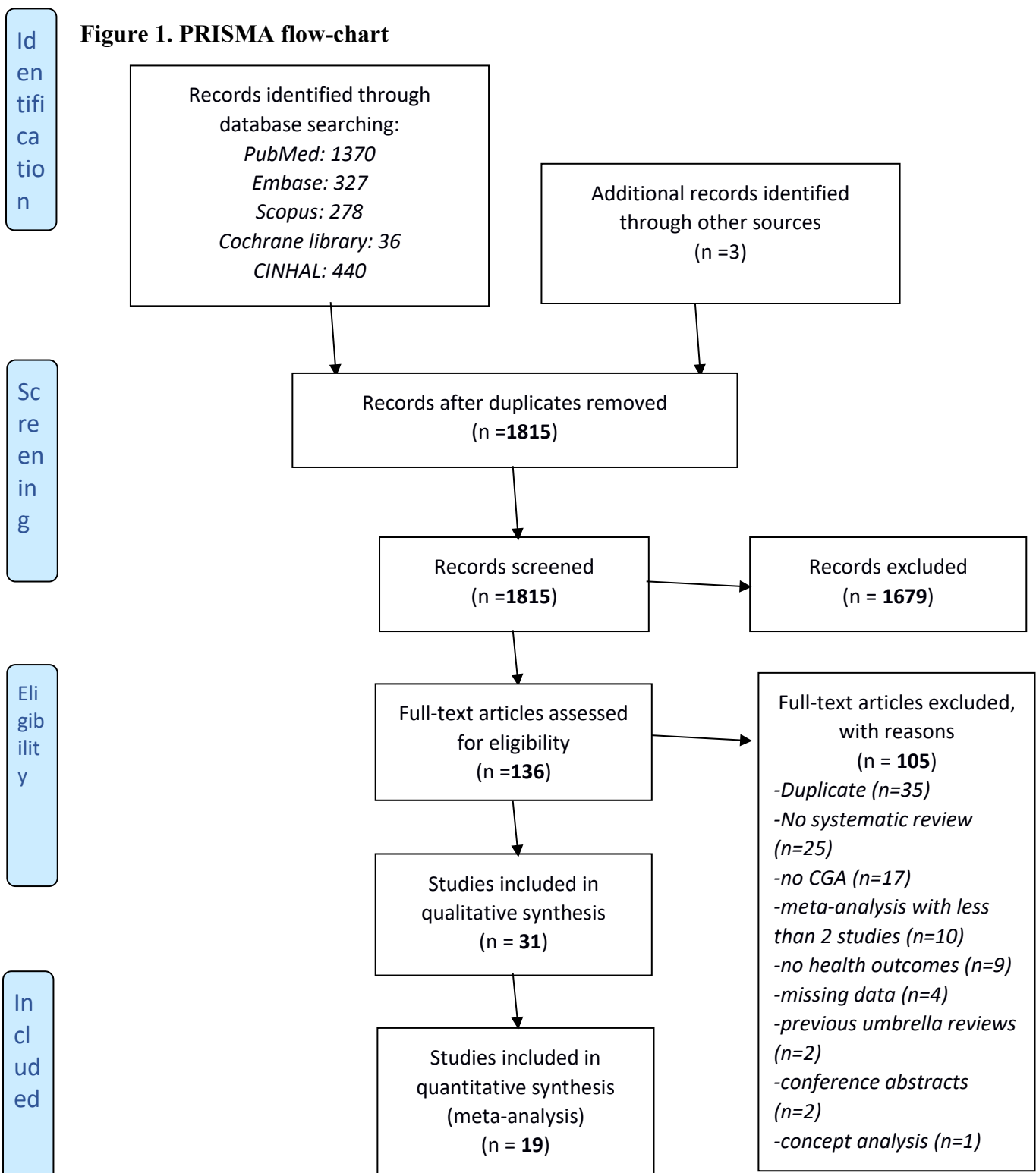
When the p-value for the random effect was < 0.05 , we evaluated the evidence derived from RCTs using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) assessment.[21] We also considered 95% prediction interval (excluding the null or not), the presence of large heterogeneity ($I^2 > 50\%$), small study effects ($P < 0.10$), and excess significance ($P < 0.10$) as possible indicators of other biases in the available evidence. Findings of the systematic reviews without meta-analysis were reported descriptively.

RESULTS

Literature review

As shown in **Figure 1**, we identified 1,815 unique manuscripts across all searched databases. After excluding 1,679 abstracts, 136 full texts were examined and a total of 31 systematic reviews were considered eligible, 19 including a meta-analysis. References of the included works are reported in **Supplementary Table 2**.

Figure 1. PRISMA flow-chart



Findings from the randomized controlled trials

As reported in **Supplementary Table 3**, the 53 outcomes included a median of six RCTs (range: 3-21) with a median of 2,088 older participants (range: 355 to 14,597) for a total of 182,214 older people. Altogether, about half of the outcomes were studied in hospital setting (26/53), 10/53 in orthopaedics, nine in surgery setting, five among community-dwellers, three in outpatients. Regarding the type of CGA used, the majority (18/53) used CGA-ward. Among the outcomes investigated, mortality was the most common explored (14/53), followed by disability (8/53), and by hospitalization/re-hospitalization (4/53) (**Supplementary Table 3**).

Overall, 13/53 (=25%) of the outcomes included reported that CGA is statistically significantly superior to usual/standard care in RCTs. **Table 1** shows the GRADE assessment of RCTs of CGA, divided by setting. In emergency surgery setting, the use of CGA was associated with lower mortality at 12 months (RR=0.70; 95%CI: 0.54-0.90; moderate strength) and time to surgery (RR=0.60; 95%CI: 0.50-0.73; low strength). In older adults admitted to a surgical service (excluding orthopaedic ward), there was moderate strength of evidence that perioperative CGA can significantly reduce delirium compared to usual/standard care (RR=0.52; 95%CI: 0.37-0.92) and length of stay in hospital of approximately two days (MD=-1.98; 95%CI: -3.09 to -0.88). In older patients with hip fracture following a trauma, CGA significantly reduced the risk of delirium (OR=0.71; 95%CI: 0.54-0.92; high strength), prevented mobility decline (SMD=0.32; 95%CI: 0.12-0.52; moderate strength), reduced mortality (OR=0.73; 95%CI: 0.54-0.98; low strength) and disability in activities of daily living [ADL] (SMD=0.26; 95%CI: 0.04-0.49; very low strength) compared to usual/standard care. In older adults admitted to hospital for acute medical condition or injury, with a high certainty of evidence CGA significantly reduced nursing home admission at discharge (RR=0.86; 95%CI: 0.75-0.89), the risk of falls (RR=0.51; 95%CI: 0.29-0.89), and pressure sores (RR=0.46; 95%CI: 0.24-0.89) (**Table 1**). Moreover, CGA increased the probability to be discharged at home after a hospitalization (RR=1.06; 95%CI: 1.009-1.10) even if supported by a moderate strength of evidence

according to the GRADE. Finally, in community-dwelling older adults, CGA reduced the risk of physical frailty (RR=0.77; 95%CI: 0.64-0.93; high strength).

Supplementary Table 3 reports the ancillary analyses for the 53 outcomes of the RCTs included in our analyses. Heterogeneity was low in 24/53 ($I^2 < 50\%$), high in 18/53 (I^2 between 50 and 75%) and very high in 11/53 outcomes. Small study effect, as p-value of the Egger's test < 0.10 , was present in 13/53 of the outcomes included, whilst the excess significance bias was present in 10/53 outcomes. The largest study reported statistically significant results in 14/53 outcomes. The prediction intervals included the null values in all the outcomes evaluated.

Supplementary Table 4 reports the quality assessment made according to the AMSTAR2. Overall, among the 19 meta-analyses included, two were rated as of high quality, four of medium, seven low quality and the others very low. Among the 12 systematic reviews included only one was rated high, two systematic reviews scored low, while the others were deemed to be critically low, as shown in **Supplementary Table 4**.

Table 1. GRADE assessment of significant associations of randomized controlled trials of comprehensive geriatric assessment

| Certainty assessment | | | | | | | Summary of findings | | | | |
|---|--------------------------|----------------------|------------------|-----------------|---|---|---------------------------------|---|--|--------------------------------------|---|
| Participa nts (studies) | Risk of bias | Inconsistenc y | Indirectne ss | Imprecisi on | Publicati on bias | Overall certaint y of evidence | Study event rates (%) | | Relativ e effect (95% CI) | Anticipated absolute effects | |
| | | | | | | | With usual/standar d care | With comprehensi ve geriatric assessment | | Risk with usual/standar d care | Risk difference with comprehensiv e geriatric assessment |
| Surgery setting | | | | | | | | | | | |
| Mortality at 12 months in older adults in surgical ward (emergency surgery) | | | | | | | | | | | |
| 4458 (4 RCTs) | not serio us | serious ^a | not serious | not serious | none | ⊕⊕⊕○ MODERA TE | 523/2932 (17.8%) | 206/1526 (13.5%) | RR 0.70 (0.54 to 0.90) | 178 per 1.000 | 54 fewer per 1.000 (from 82 fewer to 18 fewer) |
| Reduction in time to surgery in older adults in surgical ward (emergency surgery) | | | | | | | | | | | |
| 1107 (3 RCTs) | not serio us | serious ^a | not serious | not serious | publicatio n bias strongly suspected _b | ⊕⊕○○ LOW | 252/536 (47.0%) | 390/571 (68.3%) | RR 0.60 (0.50 to 0.73) | 470 per 1.000 | 188 fewer per 1.000 (from 235 fewer to 127 fewer) |
| Delirium in older adults hospitalized under nonorthopedic surgical teams for operative or nonoperative management | | | | | | | | | | | |
| 1139 (5 RCTs) | serio us ^c | not serious | not serious | not serious | none | ⊕⊕⊕○ MODERA TE | 90/536 (16.8%) | 49/603 (8.1%) | RR 0.52 (0.37 to 0.92) | 168 per 1.000 | 81 fewer per 1.000 (from 106 fewer to 13 fewer) |

Length of stay (days) in older adults hospitalized under nonorthopedic surgical teams for operative or nonoperative management

| Certainty assessment | | | | | | | Summary of findings | | | | |
|----------------------|----------------------|-------------|-------------|-------------|------|------------------|---------------------|-----|---|---|---|
| 617 (3 RCTs) | serious ^c | not serious | not serious | not serious | none | ⊕⊕⊕○ MODERATE | 264 | 353 | - | - | MD 1.98 days lower (3.09 lower to 0.88 lower) |

Orthopedics

Mobility in older adults with hip fracture trauma

| | | | | | | | | | | | |
|-----------------|-------------|----------------------|-------------|-------------|------|------------------|-----|-----|---|---|---|
| 982 (6 RCTs) | not serious | serious ^a | not serious | not serious | none | ⊕⊕⊕○ MODERATE | 495 | 487 | - | - | SMD 0.32 SD higher (0.12 higher to 0.52 higher) |
|-----------------|-------------|----------------------|-------------|-------------|------|------------------|-----|-----|---|---|---|

Delirium in older adults with hip fracture trauma

| | | | | | | | | | | | |
|------------------|-------------|-------------|-------------|-------------|------|--------------|--------------------|--------------------|----------------------------------|---------------|---|
| 1443 (6 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 313/667 (46.9%) | 283/776 (36.5%) | OR 0.71 (0.54 to 0.92) | 469 per 1.000 | 84 fewer per 1.000 (from 146 fewer to 21 fewer) |
|------------------|-------------|-------------|-------------|-------------|------|--------------|--------------------|--------------------|----------------------------------|---------------|---|

ADL in older adults with hip fracture trauma

| | | | | | | | | | | | |
|------------------|---------------------------|----------------------|-------------|-------------|------|------------------|-----|-----|---|---|---|
| 1291 (5 RCTs) | very serious ^d | serious ^a | not serious | not serious | none | ⊕○○○ VERY LOW | 648 | 643 | - | - | SMD 0.26 SD higher (0.04 higher to 0.49 higher) |
|------------------|---------------------------|----------------------|-------------|-------------|------|------------------|-----|-----|---|---|---|

Mortality in older adults with hip fracture trauma

| | | | | | | | | | | | |
|------------------|---------------------------|-------------|-------------|-------------|------|-------------|---------------------|-------------------|----------------------------------|---------------|---|
| 2088 (8 RCTs) | very serious ^d | not serious | not serious | not serious | none | ⊕⊕○○ LOW | 125/1047 (11.9%) | 91/1041 (8.7%) | OR 0.73 (0.54 to 0.98) | 119 per 1.000 | 29 fewer per 1.000 (from 51 fewer to 2 fewer) |
|------------------|---------------------------|-------------|-------------|-------------|------|-------------|---------------------|-------------------|----------------------------------|---------------|---|

Hospital

| Certainty assessment | | | | | | | Summary of findings | | | | |
|---|-------------|----------------------|-------------|-------------|------|------------------|----------------------|----------------------|---------------------------------|---------------|---|
| Institutionalization in older adults admitted to hospital at discharge | | | | | | | | | | | |
| 4459 (12 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 674/2300 (29.3%) | 579/2159 (26.8%) | RR 0.86 (0.75 to 0.99) | 293 per 1.000 | 41 fewer per 1.000 (from 73 fewer to 3 fewer) |
| Discharge at home in older adults admitted to hospital | | | | | | | | | | | |
| 6799 (16 RCTs) | not serious | serious ^a | not serious | not serious | none | ⊕⊕⊕○ MODERATE | 1852/3301 (56.1%) | 2079/3498 (59.4%) | RR 1.060 (1.009 to 1.100) | 561 per 1.000 | 34 more per 1.000 (from 5 more to 56 more) |
| Falls in older adults admitted to hospital for acute medical condition or injury | | | | | | | | | | | |
| 658 (3 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 40/469 (8.5%) | 14/189 (7.4%) | RR 0.51 (0.29 to 0.89) | 85 per 1.000 | 41 fewer per 1.000 (from 61 fewer to 9 fewer) |
| Pressure sores in older adults admitted to hospital for acute medical condition or injury | | | | | | | | | | | |
| 658 (3 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 36/469 (7.7%) | 16/189 (8.5%) | RR 0.46 (0.24 to 0.89) | 77 per 1.000 | 41 fewer per 1.000 (from 58 fewer to 8 fewer) |
| Institutionalization in older adults admitted to hospital at 3 and 6 months | | | | | | | | | | | |
| 6285 (14 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 568/3061 (18.6%) | 481/3224 (14.9%) | RR 0.80 (0.71 to 0.89) | 186 per 1.000 | 37 fewer per 1.000 (from 54 fewer to 20 fewer) |

| Certainty assessment | Summary of findings |
|----------------------|---------------------|
|----------------------|---------------------|

Non-hospital setting

Physical frailty in community-dwelling older adults

| | | | | | | | | | | | |
|-----------------|-------------|-------------|-------------|-------------|------|--------------|--------------------|--------------------|--|---------------|---|
| 786 (3 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 133/351 (37.9%) | 135/435 (31.0%) | RR 0.77 (0.64 to 0.93) | 379 per 1.000 | 87 fewer per 1.000 (from 136 fewer to 27 fewer) |
|-----------------|-------------|-------------|-------------|-------------|------|--------------|--------------------|--------------------|--|---------------|---|

Abbreviations: **CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **SMD:** Standardized mean difference; **OR:** Odds ratio

Explanations

- a. I² between 50% and 75%
- b. Egger's test (p-value)<0.05
- c. Between 10% and 30% of RCTs with a high RoB
- d. Risk of bias present in more than 30% of the RCTs

Findings from the narrative systematic reviews

Overall, twelve systematic reviews without a formal meta-analysis for a total of 97,530 participants were included (**Table 2** for intervention studies, **Table 3** for observational studies; other information in **Supplementary Table 5**). In systematic reviews of RCTs, CGA seems to lead to an improvement in quality of care in older outpatients affected by chronic conditions, whilst the effect on hospital/emergency department admission, use and costs of health services was less clear. In 3,759 nursing home residents, CGA decreased the risk of falls in 4/8 RCTs included. When considering CGA-based tools, the CGA may help the clinician to better tailor therapy and reduce mortality in 425 patients affected by non-Hodgkin lymphoma. Similarly, CGA-based tools reduced the risk of mortality in older patients undergoing surgery and with solid tumour cancer.

Table 2. Summary of Findings of the Systematic Reviews (Without Meta-analysis) included of the randomized controlled trials

| Author, year | Sample size | Surgery | Orthopedics | Hospital | Non-hospital |
|----------------|-------------|---|---------------|---|--|
| Boult, 2009 | 5,925 | Not available | Not available | Not available | Increase of quality of care in 4/4 RCTs included, quality of life, use of health care |
| Daniels 2020 | 1,143 | Reduction of length of stay in 2/4 RCTs | Not available | Not available | Not available |
| Garrad, 2019 | 1,643 | Not available | Not available | Not available | No effect of CGA on mortality and hospital/ED admission |
| Marino, 2018 | 3,382 | Not available | Not available | Not available | Reduction of ED/hospital admission in ¾ studies included |
| McCusker, 2006 | 6,606 | Not available | Not available | Little effect on ED utilization for hospital-based interventions (excluding ED-based interventions) | Reduction of ED/hospital admission in outpatient and/or primary care or home care settings |
| Neyens, 2011 | 3,759 | Not available | Not available | Not available | Reduction of falls in 4/8 RCTs in nursing home residents |

Abbreviations: RCT: randomized controlled trial; CGA: comprehensive geriatric assessment; ED: emergency department.

Table 3. Summary of Findings of the Systematic Reviews (Without Meta-analysis) included of the observational studies

| Author, year | Sample size | Surgery | Orthopedics | Hospital | Non-hospital |
|------------------|-------------|--|---------------|---|--------------------------------------|
| Caillet, 2014 | 12,900 | Optimal prediction of mortality with CGA-based tools and domains | Not available | Not available | Not available |
| De Almeida, 2015 | 58,244 | Not available | Not available | Not available | CGA captures needs of older patients |
| Graf, 2011 | 2,476 | Not available | Not available | Good discrimination of adverse outcomes in ED | Not available |
| Lin, 2016 | 815 | Optimal prediction of mortality with CGA-based tools | Not available | Not available | Not available |
| Scheepers, 2020 | 212 | Not available | Not available | CGA may help identify higher risk of non-completion of chemotherapy for frail people | Not available |
| Terret, 2015 | 425 | Not available | Not available | CGA may help identify higher risk of death for frail people and fit patients for curative therapy | Not available |

Abbreviations: CGA: comprehensive geriatric assessment; ED: emergency department.

DISCUSSION

In this umbrella review, including 31 systematic reviews and approximately 300,000 older participants, we found data on the effectiveness of CGA across different settings and conditions and toward multiple outcomes. Focusing on intervention studies we studied of the effect of CGA on 53 different outcomes including information on “hard outcomes” such as mortality, risk of hospitalization and admission to nursing home. Systematic reviews without meta-analysis completed this picture also giving information regarding the use of CGA-based tools, particularly in patients affected by cancer.

In the meta-analyses of the RCTs, we found high certainty of the evidence regarding the importance of CGA in reducing nursing home admission, risk of falls and pressure sores in hospital setting. These findings indicate that all older patients admitted to hospital should be evaluated through the CGA not only for decreasing the institutionalization, but also for decreasing other outcomes, such as falls and pressure sores, that can further increase the length of stay in hospital. These findings are of clinical importance since CGA reduced the risk of nursing home admission, falls, and pressure sores of about 41 units for every 1,000 older patients evaluated, when compared to usual/standard care, indicating that in hospital setting CGA is a highly beneficial intervention for older patients.

Moreover, our works indicated that in older patients affected by hip fracture, CGA significantly prevented delirium. Delirium is among the most frequent complication in people undergoing surgery for a hip fracture, being associated with higher rates of disability and cognitive recovery, and a prolonged hospital stay with consequent higher mortality rates and treatment costs.[22] Moreover, there is an increasing evidence that episodes of delirium may increase the risk of dementia after hospital discharge. [23, 24] Therefore, to reduce the rate of delirium in older patients affected by a hip fracture is a priority also from a public health perspective [25] and in this sense CGA seems to be highly effective when compared to usual/standard care as the evidence supporting this finding is not

affected by any bias. Furthermore, 84 fewer patients out of 1,000 patients affected by hip fracture and treated with CGA experienced delirium. Moreover, even if supported by a lower certainty of evidence, CGA seems to be beneficial in improving mobility, disability and mortality in patients with a hip fracture further supporting the benefits of an integrated care of geriatrics and orthopedics, i.e., orthogeriatric model. [26]

In the surgery setting, CGA was useful in decreasing the risk of mortality at twelve months and time to surgery in emergency, even if this evidence is supported by a high heterogeneity of the findings. Moreover, the finding that CGA can decrease the length of stay in general surgery by approximately two days is of interest, but again the poor quality of the RCTs included in this investigation did not permit to have firm conclusions regarding this outcome.

Finally, meta-analyses of the RCTs, suggested that CGA is able to significantly reduce physical frailty in community-dwelling older adults with a high certainty of evidence, further suggesting that CGA could be beneficial not only in the hospital setting, but also in primary care settings.[27] However, among the 53 outcomes included, only five included community-dwellers thus further research is needed in this setting taking hard outcomes such as mortality, nursing home admission and hospitalization as endpoints.

Narrative systematic reviews completed the picture of CGA giving some information regarding CGA-based tools in populations different from those treated in RCTs, such as outpatients having cancer. A strong limitation of this evidence is that the quality assessment of this kind of works is not possible and, therefore, we cannot distinguish high quality evidence from lower grades. Altogether these findings suggest that CGA can be used for evaluating older patients having solid tumor or hematological cancers and undergoing treatments typical of these conditions, such as chemotherapy or radiotherapy and finally indicating the role of CGA in personalized medicine in older patients. [9]

Our review is unique since it is the first comprehensive literature review of the evidence on use of CGA in different settings (i.e., hospital, outpatients, community) and its effectiveness for prevention of several relevant clinical outcomes. On the contrary, previous umbrella reviews on the same topic summarized CGA intervention definitions and benefits, only from systematic reviews and meta-analysis including interventional studies carried out in hospital setting.[5] Another review of reviews was more broadly focused on different elements of the integrated care approach for older people and among others also CGA, but did not analyze effect on clinical outcomes.[28] Both these works only provided a narrative synthesis of the evidence and thus not performing any evaluation of their strength.

We believe that our umbrella review can add some novel findings to the discussion regarding the importance of CGA in daily clinical practice. In particular, we believe that to judge several outcomes at high certainty of evidence can encourage the use of CGA in these specific areas and settings (such as hospital or orthogeriatrics). At the same time, our umbrella review indicates some promising areas of research, e.g., oncology, in which the use of CGA could be strengthened. Finally, some important topics in geriatric medicine are still not covered by scientific literature regarding CGA, i.e., palliative care. Despite the fact that CGA has been used from three decades and, as reported in our umbrella review, a large literature exists regarding its positive effects, this intervention is still under-used worldwide, probably suggesting that some obstacles are still present. A number of barriers to the implementation of CGA includes the lack of guidelines, professional and patients' factors, need for professional interactions, capacity for organizational change as well as social, political and legal factors and economic aspects.[29] In this regard, for overcoming these barriers, a better approach to research, clinical activity and teaching might be performed and encouraged by geriatricians, also in concerted actions of other health professional interested in CGA. [30]

The findings of our umbrella review must be considered within its limitations. First, the RCTs included in the systematic reviews with meta-analyses of CGA intervention are probably underpowered since small study effect and excess significance bias was present in about ¼ of outcomes included. Moreover, different definitions of CGA may influence our results in terms of clinical heterogeneity: we tried to overcome this limitation using a stringent value of $I^2 < 50\%$ for detecting this issue and for giving high certainty of evidence according to the GRADE. Similarly, the prediction intervals included the null value in all outcomes investigated, suggesting that further research is needed. Second, it is known that meta-analyses have important limitations [31] and their results may also depend on choices made about what estimates to select from each individual study and how to report them in the meta-analysis (e.g. in our umbrella review several meta-analyses did not report information regarding the type of CGA used).[31] Furthermore, applying the criteria suggested by the AMSTAR-2, we observed that several systematic reviews had low/critically low rating, mainly owing to not reporting of funding and not pre-registering protocols. Moreover, most studies on CGA focused on mortality, but the need for more studies investigating patient-centered outcomes is urgent. Perhaps among limitations or opportunities for future research. Finally, even if the GRADE is the preferred method for assessing the certainty of evidence, this assessment does not mean automatically the definition of a recommendation, such as a in guideline.

CONCLUSIONS

In this umbrella review including 19 independent meta-analyses and 53 outcomes, we found that CGA could be beneficial in the hospital setting with a high certainty of the evidence and with a less strong certainty in surgery, orthopedics and primary care settings. In older patients affected by cancer the use of CGA-based tools seems to be promising, but further intervention research is urgently needed. Overall, our findings support the use of CGA in clinical practice, also encouraging new research in different directions in which the geriatrician could be useful for tailored and personalized medicine.

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Supplementary Tables

Supplementary Table 1: Database search strategy

| | Search terms (all searches ran on 05th November 2021) |
|-----------------------------------|---|
| Pubmed | <p>("comprehensive geriatric assessment"[Title/Abstract] OR "geriatric assessment"[Title/Abstract] OR ("geriatric assessment"[MeSH Terms] OR ("geriatric"[All Fields] AND "assessment"[All Fields]) OR "geriatric assessment"[All Fields] OR ("assessment"[All Fields] AND "geriatric"[All Fields]) OR "assessment geriatric"[All Fields])) AND ("metaanaly*"[Title/Abstract] OR "metaanaly*"[Title/Abstract] OR ("systematic review"[Publication Type] OR "systematic reviews as topic"[MeSH Terms] OR "systematic review"[All Fields]))</p> <p>Total hits: 1,238</p> |
| Embase (searched via OVID) | <p>(comprehensive geriatric assessment or geriatric assessment or Assessment, Geriatric).mp. and (metaanaly* or metaanaly* or systematic review).ab,ti. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]</p> <p>Total hits: 327</p> |
| Scopus | <p>TITLE-ABS-KEY ((“comprehensive AND geriatric AND assessment” OR “geriatric AND assessment”) AND (metaanaly* OR metaanaly* OR “systematic AND review”))</p> <p>Total hits: 278</p> |
| Cochrane | <p>(comprehensive geriatric assessment OR geriatric assessment OR Assessment, Geriatric) AND (metaanaly* OR metaanaly* OR systematic review) in Title Abstract Keyword</p> <p>Total hits: 36</p> |
| CINAHL | <p>(comprehensive geriatric assessment OR geriatric assessment OR Assessment, Geriatric) AND (metaanaly* OR metaanaly* OR systematic review)</p> <p>Total hits: 440</p> |

Supplementary Table 2. References list of the systematic reviews included

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Supplementary Table 3. Summary findings of the outcomes included

| Author , Year | Population | Type of interve ntion/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y signi fica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------|--|---|--|---------------------|---------------------------|---------------------------|----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Conroy , 2011 | Frail older adults discharged rapidly (<72 h) from ED | CGA | Mortality | 5 | RR | 0.99 (0.75, 1.3) | 0.9 3 | 45. 3 | No | 1.27/0 | No | No | 0.63, 1.54 | 1117 | 1170 | 2287 |
| Conroy , 2011 | Frail older adults discharged rapidly (<72 h) from ED | CGA | Institution alization at end of follow-up | 8 | RR | 0.97 (0.83, 1.12) | 0.6 4 | 73. 5 | No | 2.36/2 | No | No | 0.68, 1.37 | 1897 | 1976 | 3873 |
| Eagles, 2020 | Older adults admitted to a trauma centre | GTC | In-hospital mortality | 6 | OR | 0.96 (0.76, 1.2) | 0.6 9 | 19. 6 | No | 3.55/1 | Yes | No | 0.59, 1.54 | 4908 | 5793 | 10701 |
| Eamer, 2017 | Older adults in surgical ward (emergency surgery) | CGA | Loss of function | 4 | RR | 0.91 (0.82, 1) | 0.0 6 | 64. 7 | No | 0.46/2 | Yes | No | 0.61, 1.35 | 714 | 679 | 1393 |

| Author , Year | Population | Type of interve nction/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------|---|--|--|---------------------|---------------------------|---------------------------|-----------------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Eamer, 2017 | Older adults in surgical ward (emergency surgery) | CGA | Mortality at discharge | 5 | RR | 0.72 (0.35, 1.5) | 0.3 8 | 40 | No | 2.7/2 | No | Yes | 0.09, 5.5 | 838 | 799 | 1637 |
| Eamer, 2017 | Older adults in surgical ward (emergency surgery) | CGA | Mortality at 12 months | 4 | RR | 0.7 (0.54, 0.9) | 0.0 06 | 51. 5 | No | 2.7/3 | No | No | 0.26, 1.88 | 1526 | 2932 | 4458 |
| Eamer, 2017 | Older adults in surgical ward (emergency surgery) | CGA | Reduction in time to surgery | 3 | RR | 0.6 (0.5, 0.73) | <0. 000 1 | 50. 1 | Yes | 1.86/3 | No | Yes | 0.08, 4.4 | 571 | 536 | 1107 |
| Eamer, 2018 | Older adults in surgical ward | CGA | Institution alization at end of follow-up | 8 | RR | 0.85 (0.69, 1.05) | 0.1 2 | 34. 8 | No | 2.17/2 | No | No | 0.51, 1.4 | 852 | 830 | 1682 |
| Ekdahl, 2015 | Frail older adults admitted to hospital | CGA- ward | Institution alization at discharge | 4 | RR | 1.13 (0.99, 1.28) | 0.0 8 | 86. 1 | No | 0.48/0 | No | Yes | 0.51, 1.72 | 631 | 626 | 1257 |

| Author , Year | Population | Type of interve ntion/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------|--|---|---------------------------------------|---------------------|---------------------------|---------------------------------|-----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Ekdahl, 2015 | Frail older adults admitted to hospital | CGA- ward | ADL | 9 | SM D | 0.062 (- 0.054, 0.178) | 0.2 93 | 55. 6 | No | 4.28/5 | No | No | -0.26, 0.38 | 2263 | 1918 | 4181 |
| Ekdahl, 2015 | Frail older adults admitted to hospital | CGA- ward | IADL | 5 | SM D | 0.004 (- 0.07, 0.08) | 0.9 2 | 43 | No | NA | NA | No | -0.12, 0.13 | 1436 | 1185 | 2621 |
| Ekdahl, 2015 | Frail older adults admitted to hospital | CGA- ward | Readmissi on at final follow-up | 6 | RR | 1.09 (0.98, 1.21) | 0.1 3 | 81. 3 | No | 1.07/1 | No | Yes | 0.82, 1.44 | 1835 | 1493 | 3328 |
| Ekdahl, 2015 | Frail older adults admitted to hospital | CGA- ward | Cognitive function | 5 | SM D | -0.005 (- 0.13,0 .12) | 0.9 3 | 64. 5 | Yes | 2.46/3 | No | No | -0.21, 0.2 | 548 | 507 | 1055 |
| Ekdahl, 2015 | Frail older adults admitted to hospital | CGA- ward | Quality of life | 3 | SM D | -0.07 (- 0.33, 0.19) | 0.6 | 81. 4 | No | 0.96/1 | No | No | -2.43, 2.29 | 190 | 165 | 355 |
| Ekdahl, 2015 | Moderately frail older adults | CGA- ward | Institution alization | 5 | RR | 1.05 (0.99, 1.12) | 0.1 1 | 70 | No | 0.43/0 | No | No | 0.91, 1.22 | 1409 | 1644 | 3053 |

| Author , Year | Population | Type of interve nction/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------|--|--|-----------------------|---------------------|---------------------------|-------------------------------|----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| | admitted to hospital | | at discharge | | | | | | | | | | | | | |
| Ekdahl, 2015 | Moderately frail older adults admitted to hospital | CGA- ward | ADL | 7 | SM D | 0.09 (- 0.001, 0.19) | 0.0 5 | 82. 7 | No | 4.57/5 | No | No | -0.16, 0.35 | 2562 | 2490 | 5052 |
| Ekdahl, 2015 | Moderately frail older adults admitted to hospital | CGA- ward | Mortality | 11 | RR | 1.06 (0.99, 1.13) | 0.1 | 73. 6 | No | 1.06/1 | No | No | 0.94,1. 11 | 2102 | 2244 | 4346 |
| Ellis, 2011 | Older adults admitted to hospital | CGA- consult | Cognitive function | 5 | SM D | 0.12 (- 0.01, 0.24) | 0.0 8 | 48 | No | 3/2.76 | No | No | -0.26, 0.49 | 1812 | 1505 | 3317 |
| Ellis, 2011 | Older adults admitted to hospital | CGA- ward | LOS | 13 | MD | 1.12 (- 1.11, 3.35) | 0.3 2 | 85. 8 | No | 4.34/0 | Yes | Yes | -7.1, 9.35 | 2052 | 1982 | 4034 |
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | Discharge to home | 16 | RR | 1.06 (1.009 , | 0.0 2 | 53. 2 | Yes | 1.46/1 | No | No | 0.97, 1.15 | 3408 | 3301 | 6709 |

| Author , Year | Population | Type of interve nction/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------|---|--|---|---------------------|---------------------------|--------------------------------|----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| | | | | | | 1.1) | | | | | | | | | | |
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | Living at home at end of follow-up (3-12 months) | 10 | RR | 1.05 (0.79, 1.38) | 0.7 5 | 59. 9 | No | 5.05/1 | Yes | No | 0.97, 1.15 | 2082 | 2224 | 4306 |
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | In-hospital mortality | 10 | RR | 1.05 (0.79, 1.38) | 0.7 5 | 59. 9 | No | 5.05/1 | Yes | No | 0.63, 1.74 | 2082 | 2224 | 4306 |
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | Mortality | 20 | RR | 1.01 (0.93, 1.09) | 0.8 7 | 0 | No | 3.01/1 | No | No | 0.93,1. 09 | 5142 | 4684 | 9826 |
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | Institution alization at discharge | 12 | RR | 0.863 (0.753 , 0.989) | 0.3 5 | 31. 9 | No | 2.8/4 | No | No | 0.78, 0.99 | 2159 | 2300 | 4459 |
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | Dependen ce | 14 | RR | 0.97 (0.9, 1.04) | 0.4 | 34. 5 | No | 2/1 | No | No | 0.89, 1.05 | 3351 | 3200 | 6551 |

| Author , Year | Population | Type of interve nction/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y signi fica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------|---|--|--|---------------------|---------------------------|--------------------------------|-----------------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | Readmissi on at final follow-up | 13 | RR | 1.02 (0.94, 1.11) | 0.6 2 | 0 | No | 1.59/1 | No | No | 0.93, 1.12 | 3501 | 3197 | 6698 |
| Ellis, 2017 | Older adults admitted to hospital | CGA- ward | Institution alization at 3 and 6 months | 14 | RR | 0.797 (0.712 , 0.893) | <0. 000 1 | 3.7 | Yes | 5.18/5 | No | No | 0.73, 0.84 | 3224 | 3061 | 6285 |
| Fox, 2012 | Older adults admitted to hospital for acute medical condition or injury | AGUC | Falls | 3 | RR | 0.51 (0.29, 0.89) | 0.0 2 | 0 | No | 1/1 | No | No | 0.01, 18.96 | 189 | 469 | 658 |
| Fox, 2012 | Older adults admitted to hospital for acute medical condition or injury | AGUC | Pressure sores | 3 | RR | 0.46 (0.24, 0.89) | 0.0 2 | 5.2 | No | 1.41/2 | no | No | 0, 48.52 | 189 | 469 | 658 |
| Hughes , 2019 | Older adults in ED | ED interve nction | Hospitaliz ation after | 6 | RR | 0.93 (0.65, 1.32) | 0.6 7 | 96. 8 | No | 3.41/3 | No | Yes | 0.26, 3.35 | 4371 | 4313 | 8684 |

| Author , Year | Population | Type of interve nion/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------|--|---|--|---------------------|---------------------------|---------------------------|-----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Hughes , 2019 | Older adults in ED | includi ng CGA ED interve nion includi ng CGA | the index visit ED return visit | 9 | RR | 0.99 (0.8, 1.24) | 0.9 9 | 91. 7 | Yes | 3.59/1 | Yes | Yes | 0.49, 2.06 | 4814 | 4771 | 958 |
| Huss, 2008 | Community -dwelling older adults | MPHP | Functional decline | 16 | OR | 0.89 (0.77, 1.03) | 0.1 16 | 52. 5 | No | 5.84/5 | No | No | 0.56, 1.43 | 4278 | 4056 | 8334 |
| Huss, 2008 | Community -dwelling older adults | MPHP | Mortality | 21 | OR | 0.92 (0.8, 1.05) | 0.1 99 | 36 | No | 8.65/4 | Yes | No | 0.63, 1.34 | 7349 | 7248 | 14597 |
| Huss, 2008 | Community -dwelling older adults | MPHP | Institution alization | 16 | OR | 0.86 (0.68, 1.1) | 0.2 3 | 70. 9 | No | 9.93/3 | Yes | No | 0.45, 1.68 | 6099 | 5910 | 12009 |
| Kuo, 2004 | Outpatient older adults | CGA | Mortality | 9 | RR | 0.96 (0.82, 1.12) | 0.5 8 | 53. 1 | Yes | 2.8/1 | No | No | 0.79, 1.15 | 1885 | 1865 | 3750 |

| Author , Year | Population | Type of interve ntion/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------------|--|---|---|---------------------|---------------------------|------------------------------|-----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Lin, 2020 | Older adults with hip fracture trauma | CGC | Mortality at 12 months | 5 | OR | 0.76 (0.55, 1.04) | 0.0 9 | 0 | No | 1.56/0 | No | No | 0.45, 1.27 | 677 | 676 | 1353 |
| Lin, 2020 | Older adults with hip fracture trauma | CGC | Mortality | 8 | OR | 0.73 (0.54, 0.98) | 0.0 3 | 0 | No | 4.4/2 | No | No | 0.5, 1.05 | 1041 | 1047 | 2088 |
| Lin, 2020 | Older adults with hip fracture trauma | CGC | ADL | 5 | SM D | 0.26 (0.04, 0.49) | 0.0 2 | 71. 8 | No | 3.02/4 | No | No | -0.51, 1.04 | 643 | 648 | 1291 |
| Lin, 2020 | Older adults with hip fracture trauma | CGC | LOS | 9 | SM D | 0.96 (- 0.11, 2.02) | 0.0 8 | 99. 2 | Yes | 4.99/5 | No | Yes | -3.08, 4.99 | 1121 | 1129 | 2250 |
| Lin, 2020 | Older adults with hip fracture trauma | CGC | Institution alization at discharge | 5 | OR | 0.86 (0.35, 2.14) | 0.7 5 | 41. 9 | Yes | 3.37/1 | Yes | Yes | 0.07, 11.21 | 450 | 593 | 1043 |
| Macdo nald, 2020 | Community -dwelling older adults | CGA | Frailty status | 3 | RR | 0.77 (0.64, 0.93) | 0.0 06 | 38. 3 | No | 0.67/1 | No | No | 0.23, 2.57 | 435 | 351 | 786 |

| Author , Year | Population | Type of interve ntion/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|------------------------|--|---|--------------------------|---------------------|---------------------------|---------------------------|-----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| | | | (Fried criteria) | | | | | | | | | | | | | |
| Michae l, 2010 | Community -dwelling older adults | CGC | Falls | 6 | RR | 0.89 (0.76, 1.03) | 0.1 2 | 73. 1 | No | 1.21/2 | No | No | 0.54, 1.44 | 1008 | 1002 | 2010 |
| Mukher jee, 2020 | Older adults with hip fracture trauma | OGC | In-hospital mortality | 4 | OR | 0.89 (0.35, 2.27) | 0.8 | 37. 3 | Yes | 2.09/1 | No | No | 0.03, 27.72 | 513 | 530 | 1043 |
| Nordstr om, 2018 | Older adults with hip fracture trauma | GTR | Mobility | 6 | SM D | 0.32 (0.12, 0.52) | 0.0 02 | 55. 6 | No | 3.21/3 | No | Yes | -0.26, 0.5 | 487 | 495 | 982 |
| Nordstr om, 2018 | Older adults with hip fracture trauma | GTR | Discharge to home | 6 | RR | 1.07 (0.99, 1.17) | 0.0 9 | 0 | No | 0.47/0 | No | Yes | 0.96, 1.21 | 707 | 726 | 1433 |
| Nordstr om, 2018 | Older adults with hip fracture trauma | GTR | Survival | 7 | RR | 1.02 (0.99, 1.06) | 0.1 6 | 0 | Yes | 0.38/0 | No | No | 0.98, 1.07 | 862 | 880 | 1742 |

| Author , Year | Population | Type of interve nction/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y sign ifica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|-----------------------------|-------------------------------------|--|-----------|---------------------|---------------------------|--------------------------------|-----------------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Thillain adesan, 2020 | Older adults in surgical ward | periope rative multico mpone nt inpatie nt geriatri c progra m | LOS | 3 | MD | -1.98 (- 3.09, -0.88) | <0. 000 1 | 0 | No | NA | NA | Yes | -9.14, 5.18 | 353 | 264 | 617 |
| Thillain adesan, 2020 | Older adults in surgical ward | periope rative multico mpone nt inpatie nt geriatri c progra m | Delirium | 5 | RR | 0.52 (0.37, 0.92) | 0.0 2 | 39. 6 | Yes | 3.41/3 | No | Yes | 0.04, 4.28 | 603 | 536 | 1139 |
| Thillain adesan, 2020 | Older adults in surgical ward | periope rative CGA | Mortality | 3 | RR | 1.89 (0.98, 3.66) | 0.0 6 | 12. 7 | No | 2.22/0 | Yes | No | 0.01, 312.07 | 286 | 317 | 603 |

| Author , Year | Population | Type of interve nction/ CGA tools | Outcome | N of studie s | Typ e of met ric | Mean ES (LL, UL) | P | I ² | Small study effects present ? | Expecte d/Obser ved significa nt studies | Excess significa nce bias present? | Lar gest stud y signi fica nt? | 95% LLPI, ULPI | Rand omize d to CGA | Randomi zed to usual/stan dard care | Sample size |
|-----------------------------|--|--|---|---------------------|---------------------------|---------------------------|-----------|----------------|---|---|---|--|----------------------|------------------------------|--|----------------|
| Thillain adesan, 2020 | Older adults in surgical ward | preoper ative CGA | Istituziona lization at discharge | 4 | RR | 1.02 (0.55, 1.88) | 0.9 6 | 71. 3 | No | 2.21/1 | No | Yes | 0.08, 13.5 | 337 | 366 | 703 |
| Wang, 2017 | Older adults with hip fracture trauma | CGA | Delirium | 6 | OR | 0.71 (0.54, 0.92) | 0.0 09 | 25. 4 | Yes | 2.19/2 | No | No | 0.39, 1.27 | 776 | 667 | 1443 |
| Xue, 2018 | Gastrointest inal cancer older adults | CGA | Cognitive status | 3 | OR | 1.14 (0.9, 1.44) | 0.2 8 | 7.8 | Yes | NA | NA | No | 0.21, 6.28 | NA | NA | 497 |
| Xue, 2018 | Gastrointest inal cancer older adults | CGA | Depressio n | 3 | OR | 1.18 (0.9, 1.55) | 0.2 4 | 0 | No | NA | NA | No | 0.2, 6.9 | NA | NA | 497 |

Abbreviations: ADL: activity of daily living; AGUC: acute geriatric unit care; CGA: comprehensive geriatric assessment; CGC: comprehensive geriatric care; GTC: geriatric trauma consultation; GTR: geriatric team rehabilitation; ED: emergency department; ES: effect size; LL: lower limit; LLPI: lower limit prediction interval; LOS: length of stay; MD: mean difference; MPHP: Multidimensional preventive home-visit program; OGC: orthogeriatric care; OR: odds ratio; RR: risk ratio; SMD: standardized mean difference; UL: upper limit; ULPI: upper limit prediction interval.

Supplementary Table 4. AMSTAR 2 quality assessment of meta-analyses included

| Author, Year | AMSTAR 2 items ^{a, c} | | | | | | | | | | | | | | | | |
|---------------------|--------------------------------|----------------|---|----------------|---|---|----------------|---|----------------|----|-----------------|----|-----------------|----|-----------------|----|----------------|
| Meta-analyses | 1 | 2 ^b | 3 | 4 ^b | 5 | 6 | 7 ^b | 8 | 9 ^b | 10 | 11 ^b | 12 | 13 ^b | 14 | 15 ^b | 16 | Overall rating |
| Conroy 2011 | Y | N | Y | Y | N | Y | N | Y | Y | N | Y | Y | Y | Y | Y | Y | CL |
| Deschodt 2013 | Y | Y | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Y | Y | Y | Y | L |
| Eagles 2019 | Y | Y | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Y | Y | N | Y | L |
| Eamer, 2017 | Y | PY | Y | Y | Y | Y | y | Y | Y | N | Y | Y | Y | Y | Y | Y | M |
| Ekdahl 2015 | Y | Y | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Y | Y | Y | Y | L |
| Ellis, 2017 | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | H |
| Fox, 2012 | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | M |
| Hughes 2019 | Y | N | Y | Y | Y | N | N | Y | Y | N | Y | Y | Y | Y | Y | Y | CL |
| Huss 2008 | Y | N | Y | Y | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | CL |
| Kuo 2004 | Y | N | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Y | Y | Y | Y | CL |
| Macdonald, 2020 | Y | PY | N | Y | Y | N | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | L |
| Micheal 2010 | Y | Y | Y | Y | Y | N | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | CL |
| Mukherjee 2019 | Y | Y | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Y | Y | Y | Y | L |
| Nordstrom, 2018 | Y | N | Y | Y | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | M |
| Shu Ni Lin, 2020 | Y | PY | Y | Y | Y | Y | PY | Y | Y | N | Y | Y | Y | Y | Y | Y | M |
| Thillainadesan 2020 | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | H |

| Author, Year | AMSTAR 2 items ^{a, c} | | | | | | | | | | | | | | | | |
|--------------------|--------------------------------|----------------|---|----------------|---|---|----------------|---|----------------|----|-----------------|------|-----------------|----|-----------------|----|----------------|
| Meta-analyses | 1 | 2 ^b | 3 | 4 ^b | 5 | 6 | 7 ^b | 8 | 9 ^b | 10 | 11 ^b | 12 | 13 ^b | 14 | 15 ^b | 16 | Overall rating |
| Wang, 2017 | Y | N | Y | PY | Y | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | L |
| Xue 2018 | Y | N | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Y | Y | Y | Y | L |
| Systematic reviews | 1 | 2 ^b | 3 | 4 ^b | 5 | 6 | 7 ^b | 8 | 9 ^b | 10 | 11 ^b | 12 | 13 ^b | 14 | 15 ^b | 16 | Overall rating |
| Boult 2009 | Y | N | Y | Y | Y | N | N | N | N | N | N MA | N MA | N | N | N MA | Y | CL |
| Caillet 2014 | Y | N | N | N | Y | Y | N | N | N | N | N MA | N MA | N | N | N MA | Y | CL |
| Daniels 2020 | Y | Y | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Y | Y | Y | Y | H |
| De Almeida 2015 | N | N | Y | Y | Y | N | N | Y | Y | N | N MA | N MA | N | N | N MA | Y | CL |
| Garrad 2019 | Y | N | Y | Y | Y | Y | N | N | N | N | N MA | N MA | N | Y | N MA | Y | CL |
| Graf 2011 | Y | N | Y | N | N | N | N | N | N | N | N MA | N MA | N | N | N MA | Y | CL |
| Lin 2016 | Y | N | Y | Y | Y | Y | N | Y | Y | N | N MA | N MA | Y | Y | N MA | Y | L |
| Marino 2018 | Y | Y | Y | Y | N | N | N | Y | Y | N | N MA | N MA | N | N | N MA | Y | CL |

| Systematic reviews | 1 | 2^b | 3 | 4^b | 5 | 6 | 7^b | 8 | 9^b | 10 | 11^b | 12 | 13^b | 14 | 15^b | 16 | Overall rating |
|---------------------------|----------|----------------------|----------|----------------------|----------|----------|----------------------|----------|----------------------|-----------|-----------------------|-----------|-----------------------|-----------|-----------------------|-----------|-----------------------|
| McCusker 2006 | Y | Y | Y | Y | Y | Y | N | N | N | N | N MA | N MA | N | N | N MA | Y | CL |
| Neyens 2011 | Y | N | Y | Y | Y | Y | N | N | N | N | N MA | N MA | N | N | N MA | Y | CL |
| Scheepers 2020 | Y | N | Y | N | Y | N | N | Y | Y | N | N MA | N MA | N | N | N MA | Y | L |
| Terret 2015 | Y | N | Y | N | N | N | N | N | N | N | N MA | N MA | Y | Y | N MA | Y | CL |

Notes:

1. Did the research questions and inclusion criteria for the review include the components of PICO (Population, Intervention, Comparator group, Outcome)? YES/NO. For yes, must have all four.
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? YES, PARTIAL YES, NO. For Partial YES: the authors state that they had a written protocol or guide that included ALL the following (review question(s), a search strategy, inclusion/exclusion criteria, a risk of bias assessment). For YES: as for partial yes, plus the protocol should be registered and should also have specified: a meta-analysis/synthesis plan, if appropriate, and a plan for investigating causes of heterogeneity, justification for any deviations from the protocol.
3. Did the review authors explain their selection of the study designs for inclusion in the review? YES/NO. For YES, the review should satisfy one of the following: explanation for including only RCTs, or explanation for including only NRSI, or explanation for including both RCTs and NRSI.
4. Did the review authors use a comprehensive literature search strategy? YES, PARTIAL YES, NO. for PARTIAL YES must have all of the following: searched at least 2 databases (relevant to research question), provided key word and/or search strategy, justified publication restrictions (eg. Language). For YES should also have all of the following: searched the reference lists/biographies of included studies, searched trial/study registries, included/consulted content experts in the field, searched for grey literature where relevant, conducted search within 24 months of completion of the review.
5. Did the review authors perform study selection in duplicate? YES/NO. for YES, either ONE of the following: at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 per cent) with the remainder selected by one reviewer.

6. Did the review authors perform data extraction in duplicate? YES/NO. For YES, either one of the following: at least two reviewers achieved consensus on which data to extract from included studies OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 per cent) with the remainder extracted by one reviewer.
7. Did the review authors provide a list of excluded studies to justify the exclusions? YES, PARTIAL YES, NO. FOR partial yes must provide a list of all potentially relevant studies that were read in full text form but excluded from the review. For YES must also have justified the exclusion from the review of each potentially relevant study.
8. Did the review authors describe the included studies in adequate detail? YES, PARTIAL YES, NO. For PARTIAL YES, must describe all of the following: populations, interventions, comparators, outcomes, research designs. For YES should also have all of the following: described populations in detail, described intervention and comparator in detail (including doses where relevant), described study setting, timeframe or follow-up.
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? For RCTs: YES, PARTIAL YES, NO, INCLUDES ONLY NRSI. For PARTIAL YES must have assessed RoB from unconcealed allocation and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality); for YES must also have assessed RoB from allocation sequence that was not truly random and selection of the reported result from among multiple measurements or analyses of a specified outcome. For NRSI (Non Randomized Studies of Intervention): YES, PARTIAL YES, NO, INCLUDES ONLY RCTs. For PARTIAL YES must have assessed RoB from confounding and from selection bias. For YES, must also have assessed methods used to ascertain exposures and outcomes, and selection of the reported results from among multiple measurements or analyses of a specified outcome.
10. Did the review authors report on the sources of funding for the studies included in the review? YES/NO. For YES: must have reported on the sources of funding for individual studies included in the review. Note: reporting that the reviewers looked for this information but it was not reported by study authors also qualifies
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results? For RCTs: YES, NO, NO META-ANALYSIS. For YES: the authors justified combining the data in a meta-analysis and they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present and investigated the causes of heterogeneity. For NRSI: YES, NO, NO META-ANALYSIS CONDUCTED. For YES: the authors justified combining the data in a meta-analysis and they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present, and they statistically combined effects estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available, and they reported separate summary estimates for RCTs and NRSI separately when both were included in the review.
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? YES, NO, NO META-ANALYSIS INCLUDED. For YES: included only low risk of bias RCTs or, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analysis to investigate possible impact of RoB on summary estimates of effect.
13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review? YES/NO. for YES: included only low risk of bias RCTs or, if RCTs with moderate or high RoB, or NRSI were included, the review provided a discussion of the key impact of RoB on the results

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? YES/NO. For Yes: there was no significant heterogeneity in the results OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? YES, NO, NO META-ANALYSIS CONDUCTED. For YES: performed graphical statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? YES/NO. For Yes: the authors reported no competing interests OR the authors described their funding sources and how they managed potential conflicts of interest.

d Rating overall confidence in the results of the review:

HIGH: no on one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest

MODERATE: more than one non critical weakness (multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence): the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review

LOW: one critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest

CRITICALLY LOW: more than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

Supplementary Table 5. Detailed findings of the systematic reviews, without formal meta-analysis, included

| General characteristics | | | | Outcomes | | | | | | | | | | | |
|-----------------------------|-------------|---|-----------|-----------------------|------------------|------------|-------|-----------------|-----------------|----------------|------------------------|-------------------------|--|-------------------------|----------------------|
| Author, year | Sample size | Population | Mortality | Hospital/ED admission | Adverse outcomes | Disability | Falls | Quality of life | Quality of care | Length of stay | Use of Health Services | Cost of Health Services | Complications Rate | Needs of older patients | Treatment compliance |
| <i>Intervention studies</i> | | | | | | | | | | | | | | | |
| Boult, 2009 | 5,925 | Older outpatients with chronic conditions | | | | | | ↑ 7/10 | ↑ 4/4 | | ↓ 4/9, ↑ 3/9 | ↑ 1/5 | | | |
| Daniels, 2020 | 1,143 | Older patients undergoing elective abdominal cancer surgery | | | | | | | | ↓ 2/4 | | | ↓ 1/4, but with higher incidence of delirium | | |
| Garrard, 2019 | 1,643 | Older adults in primary care practice | No effect | No effect | | | | | | | | | | | |
| Marino, 2018 | 3,382 | Community-dwelling older adults | | ↓ 3/4 | | | | | | | | | | | |

| General characteristics | | | | Outcomes | | | | | | | | | | | |
|---|--------------------|---|---|--|---------------------|----------------|-----------|------------------------|------------------------|-----------------------|--------------------------------------|--|---------------------------|--|---------------------------------|
| Author, year | Sam ple size | Populati on | Mortality | Hospital/ ED admission | Adverse outcomes | Disabil ity | Fal ls | Quali ty of life | Quali ty of care | Leng th of stay | Use of Healt h Servi ces | Cost of Healt h Servi ces | Complicati ons Rate | Needs of older patients | Treatme nt complian ce |
| McCusker, 2006 | 6,606 | Older adults from different settings (excluding ED) | | Little effect on ED utilization for hospital-based interventions; ↓ ED utilization in outpatient and/or primary care or home care settings | | | | | | | | | | | |
| Neyens, 2011 | 3,759 | Nursing home residents | | | | | ↓ 4/8 | | | | | | | | |
| Observational studies using CGA-based tools | | | | | | | | | | | | | | | |
| Terret, 2015 | 425 | Patients with non-Hodgkin lymphoma | CGA may help identify higher risk of death for frail or | | | | | | | | | | | CGA may help identify fit patients for | |

| General characteristics | | | | Outcomes | | | | | | | | | | | |
|-------------------------|-------------|--|----------------|-----------------------|------------------|------------|-------|-----------------|-----------------|----------------|------------------------|-------------------------|--------------------|---|--|
| Author, year | Sample size | Population | Mortality | Hospital/ED admission | Adverse outcomes | Disability | Falls | Quality of life | Quality of care | Length of stay | Use of Health Services | Cost of Health Services | Complications Rate | Needs of older patients | Treatment compliance |
| | | | unfit patients | | | | | | | | | | | curative therapy | |
| De Almeida, 2015 | 58,244 | Community-dwelling older adults | | | | | | | | | | | | The interRAI HC instrument is able to measure outcomes and evaluate interventions effects | |
| Scheepers, 2020 | 212 | Older patients with hematologic malignancies | | | | | | | | | | | | | Higher treatment non-completion in CGA-based frail patients. Dependency, mobility impairment, cognitive dysfunction, and |

| General characteristics | | | | Outcomes | | | | | | | | | | | |
|-------------------------|-------------|--------------------------------------|---|-----------------------|--|------------|-------|-----------------|-----------------|----------------|------------------------|-------------------------|---|---|--|
| Author, year | Sample size | Population | Mortality | Hospital/ED admission | Adverse outcomes | Disability | Falls | Quality of life | Quality of care | Length of stay | Use of Health Services | Cost of Health Services | Complications Rate | Needs of older patients | Treatment compliance |
| Graf, 2011 | 2,476 | Older adults in emergency department | | | Good discrimination power of CGA in ED | | | | | | | | | | malnutrition were associated with treatment non-completion |
| Lin, 2016 | 815 | Older adults undergoing surgery | All studies showed a significant association with CGA-based frailty | | | | | | | | | | 2/4 studies showed significant association with CGA-based frailty | | |
| Caillet, 2014 | 12,900 | Older adults with solid cancer | Dependency, mobility impairment, cognitive dysfunction, | | | | | | | | | | Dependency, mobility impairment, and CGA as a whole predicted postoperative | CGA identified unrecognized health problems capable of interfering with | |

| General characteristics | | | | Outcomes | | | | | | | | | | | |
|-------------------------|--------------------|----------------|---|----------------------------------|---------------------|----------------|-----------|------------------------|------------------------|-----------------------|--------------------------------------|--|---------------------------|--|---------------------------------|
| Author, year | Sam ple size | Populati on | Mortality | Hospital/ ED admissio n | Adverse outcomes | Disabil ity | Fal ls | Quali ty of life | Quali ty of care | Leng th of stay | Use of Healt h Servi ces | Cost of Healt h Servi ces | Complicati ons Rate | Needs of older patients | Treatme nt complian ce |
| | | | depressive mood, malnutriti on, and comorbidi ties were associated with mortality independe ntly from cancer parameter s | | | | | | | | | | complicatio ns | cancer treatment. CGA results influence d 21%– 49% of treatment decisions. | |

Abbreviations: CGA: Comprehensive Geriatric Assessment; ED: Emergency Department; interRAI HC: interRAI Home Care

PRISMA checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|-------------------------|--------|--|---------------------------------|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review. | 1 |
| ABSTRACT | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | 3 |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | 5 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 5 |
| METHODS | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 6 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | 6 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Supplementary Material |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | 6 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | 6 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | 6-7 |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any | 6-7 |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|-------------------------------|--------|---|---------------------------------|
| | | assumptions made about any missing or unclear information. | |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | 7 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | 7-8 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | 7-8 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | 7-8 |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | 7-8 |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | 7-8 |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | 7-8 |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | 7-8 |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | 7-8 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | 8 |
| RESULTS | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | 9 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Figure 1 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Supplementary Material; |
| Risk of bias in | 18 | Present assessments of risk of bias for each included study. | 9-11 |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|-------------------------------|--------|--|---------------------------------|
| studies | | | |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Tables; 9-11 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | 9-11 |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | 9-11 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | 9-11 |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | 9-11 |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | 9-11 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | 9-11 |
| DISCUSSION | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | 12 |
| | 23b | Discuss any limitations of the evidence included in the review. | 14 |
| | 23c | Discuss any limitations of the review processes used. | 14 |
| | 23d | Discuss implications of the results for practice, policy, and future research. | 15 |
| OTHER INFORMATION | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | 4 |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | 4 |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | 4 |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | 8 |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|--|--------|--|---------------------------------|
| Competing interests | 26 | Declare any competing interests of review authors. | 16 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | 16 |

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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